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Clinico-Pathological Evaluation of Oral Mucocutaneous Diseases

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Abstract

The oral mucous membrane is often affected by oral mucocutaneous diseases (MCDs) as a heterogeneous group of disorders, and histopathology is the principal criterion for diagnosis of it. This study had aimed to compare the clinical evaluation of oral mucocutaneous diseases with histopathological diagnosis. The Department of Dermatology, Venerology and Pathology, Bangabandhu Sheik Mujib Medical University (BSMMU), Dhaka, carried out a future-oriented observational study. The study was conducted between July 2019 and October 2020 in 65 patients clinically diagnosed with mucocutaneous oral disorders. All the patients of dermatologic diseases with oral manifestations were selected for histopathological examination. It was observed in this study that majority (80.0%) of the patients was in inflammatory group, followed by 11(16.9%) autoimmune disease and 2(3.1) malignant disease group. Based on clinical diagnosis, among 65 patients, more than half (52.31%) patients had oral lichen planus, followed by 18(27.7%) erythema multiforme, 5(7.7%) pemphigus vulgaris, 3(4.6%) discoid lupus erythematosus, 2 (3.1) pemphigoid group, 1(1.5%) systemic lupus erythematosus and 2 (3.08%) had squamous cell carcinoma. Building on historical findings from autoimmune disorders, nine true positive cases were identified, two false positive, two false negative ones and 52 true negative ones. On the other hand, the histological findings found 1 genuine positive patient, 0 false negative patient and 63 true negative malignant patients. Finally, 50, 3, 2 and 10 patients demonstrated really positive, false positive and false negative histological findings based on inflammatory illnesses. correspondingly Inflammatory disorders. The clinical symptoms and histological results of mucocutaneous oral disorders had statistical meaning ($p<.05$). The 45 (69.23%) patients with oral lichen planus, erythema multiforme, pemphigus vulgaris, pemphius group and squamous cell carcinome showed buccal mucosa involvement with 31, 9, 2 and 2 patients, respectively. Moreover, 7 (10.76%), 6 (9.23%), 5 (7.69%) and 2 (3.07%) were also involved, respectively, in individuals who had tongue, gingiva, lip and palate. It is possible to infer that clinical diagnosis cannot be utilised as a trusted tool to diagnose mucocutaneous disorders and hence histological investigation should be carried out in the majority of cases to plan the proper management.

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1. Introduction

The clinical manifestations of dermatological diseases can be noticed from both the skin and mucous membrane lesions [1]. Inside the mouth, there is a mucous membrane called "oral mucosa" which is always affected by a variety of diseases, including mucocutaneous disorders [2]. Dermatoses, now, form a profound interest among scientists and odontological society as it is assumed that oral lesions can only be the precursor of long-term diseases related to the oral cavity. Lichen planus, lupus erythematosus, erythema multiforme, pemphigus vulgaris and hence the pemphigoid lesion groups [3] are the most important expressive disorders in this regard. History, clinical characteristics and histology are the key to diagnosis of such diseases. Diagnostic challenges result from oral mucocutaneous damage, because these lesions are similar and regular tissue biopsies may only diagnose non-specific inflammation.

Approximately 0.22 to 5 percent of the world's population is estimated to experience a severe skin and mucosal inflammatory disease called Lichen Planus (LP), which shows some 60 percent of the symptoms of oral cavity, since this disease affects different areas of the mouth cavity, including mouth mucosa, language, lips, gingiva, and often palate and body of the mouton [5]. The lesions of the intraoral lupus erythematosus are also found in the hard palate, mouth mucosa, lips and gingiva [6,7] and therefore present as the lichen planus in the mouth [8]. The first clinical symptom in oral mucosa is generally developed by another auto-immune disease called phemphigus vulgaris [9, 10, 11], overlapping with oral lichen planus medical feature [2]. Furthermore, in oral leukoplactic [2] and in oral epithelial dysplasia or squamous cell carcinoma, lichenoid characteristics might be seen clinically. As such, it is difficult to segregate from one another clinically due to the same oral Lichen Planus (LP) and another oral mucocutaneous disease criteria.

Although interface mucositis is a distinctive criterion of the oral lichen planus, the disease has a range of characteristics under the microscope including hydropic degeneration, epithelial and basal belt-like cells and predominantly T-lymphocyte infiltration, of basals with dispersed dyskeratotic keratinocytes [12]. In histological exams of oral lupus erythematosus, interface mucositis and perivascular inflammatory infiltrate may also be observed [13]. In this disease under a Microscope, it is also possible to detect a thicker basement membrane and epithelium ranging from atrophic to

hyperplastic with keratin plugging.[13]. The epithelium, like sub-epithelial clefting [14], also includes the histological characteristics of the mucous membrane pemphigoid.

A tissue investigation of oral epithelial dysplasia shows that basal cells like the oral planus lichen (OLP) are subject to a substantial chronic inflammatory infiltrate [2]. In addition, interface mucositis is a reminder of the histological landmark OLP in verrucous proliferative leukoplakia biopsies. Since different types of mucosal diseases exhibit very alike features histologically that arise confusion to the pathologist for evaluating it properly. Therefore, this study sought to compare the clinical evaluation of oral mucocutaneous diseases with histopathological diagnosis for providing some annotations towards the related health professionals.

2. Materials and Methods

This study was carried out at Bangabandhu Sheik Mujib Medical University (BSMMU), Dhaka. This study was undertaken in the department of Dermatics and Venereology and Pathology. The study was place in 65 clinically diagnosed individuals with oral mucocutaneous disorders between July 2019 and October 2020. For histological analysis, all dermatological patients with oral symptoms have been selected. The objective of this study was the clinical examination and histological correlation of oral muco-cutaneous disorders. The patient's age and sex, clinical data on location and accompanying symptoms were recorded in this investigation. For histopathology, all dermatologically diagnosed patients with oral symptoms were selected. In all participants with oral lesion, biopsy specimens were collected from the lesional or perilesional area. Punch biopsy was used mostly for oral mucosal biopsy. A plastic handle with a diameter of 2-8 mm and a gradient of 0,25-0.50 mm was available [15]. The instrument was made from a cylindrical bladder. This eliminated a core tissue from which the basis has been removed with curved scissors or a knife, and avoided the typical procedure used to hold the specimen using toothed tissue forceps [15]. Otherwise, blunt forceps were utilised to grab the tissue and grab the tissues from a major site of interest [15] instead of toothed forceps. Local anaesthetic was administered to prevent the artefacts in the sample for the biopsy operation from the lesion [15].

If block anaesthesia cannot occur, infiltration was given as cardinal reference (top, bottom, left, right) at least 3-4 mm distant from the lesion and four-point anesthetytic techniques were utilised [15]. Intralesional injection of the anaesthetic solution was avoided, because this results in a haemorrhage with extravasation and spinal cord separation, the bigger the sample the haemorrhage,

the more precise diagnostic, and the larger the biopsy was possible. [15]. The haemorrhage was prevented.

The samples were brought to the Pathology Department of the University of Sheik Mujib, Bangabandhu, to Dhaka by the BSMMU (H and E). The participants in this study comprised patients with clinical diagnoses such as lichen planus, lupus erythematosus, erythema multiforme, pemphigus vulgaris, pemphigoid disease group, and oral squamous cell carcinoma. Diseases which most typically develop in oral lesions because of the presence of a variety of diseases were picked to focus on. The present study eliminated patients who did not want to participate willingly, and who did not have a definite diagnosis of the illnesses indicated above. The authority responsible and the participants requested the necessary approval. Every patient was properly informed about the risks and benefits of this study before the data was collected and informed that he had the right to withdraw from the trial at all times. All patients were kept anonymous for the whole trial.

Furthermore, all selected subjects had written approval before the trial. To maintain data on patients, a pre-designed case record form was employed. For data analysis, the Social Science Statistical Package (SPSS) was used.

3. Results

Table I shows demographic variable of the study participants, it was observed that almost (41.54%) of the patients belonged to age of 41-50 years and almost two third (61.5%) of patients were male.

Table I: Distribution of the study patients by demographic variable (n=65)

Demographic variable	Number of patients	Percentage
Age		
21-30	14	21.54

31-40	24	36.92
41-50	27	41.54
Sex		
Male	40	61.53
Female	25	38.47

Table II shows clinical diagnosis of the study patients, it was observed that more than half (52.31%) of patients had oral lichen planus where 18(27.7%), 5(7.7%), 3(4.6%), 2(3.1), 1(1.5%) and 2 (3.1%) had erythema multiforme, pemphigus vulgaris, discoid lupus erythematosus, pemphigoid group, systemic lupus erythematosus and squamous cell carcinoma, respectively.

Table II: Distribution of the study patients by clinical diagnosis (n=65)

Clinical diagnosis	Number of patients	Percentage
Inflammatory lesions		
Oral lichen planus	34	52.31
Erythema multiforme	18	27.69
Autoimmune disease		
Pemphigus vulgaris	5	7.69
Discoid lupus erythematosus	3	4.61
Pemphigoid group	2	3.08
Systemic lupus erythematosus	1	1.54
Malignant disease		
Squamous cell carcinoma	2	3.08

Table III illustrates the comparison of clinical diagnosis and histopathology findings of autoimmune, malignant and inflammatory diseases. Based on clinical diagnosis, 9 reals positive, 2 fake positive and 2 false negative cases were reported in autoimmune illnesses while 52 were true negative, based on histological findings. Chi-square tests were conducted and statistically important ($p<0.01$) were found. On the other hand, it has been shown that there are true positive cases, false positive 1 case, false negative cases 0, and true negative cases 63, among clinically diagnosed disorders with histological findings. Chi-square tests were performed and statistically significant ($p<0.01$) were found. In addition, true positive 50, false positive 3, false negative 3, and true negative 10 cases have been found among clinically diagnosed inflammatory illnesses by histological findings. Chi-square test was done and found statistically significant ($p<0.01$).

Table III: Comparison of clinical diagnosis of autoimmune diseases with histopathology(n=65)

Clinical Diagnosis	**Histopathological findings**		**Total**	**Statistics**
	Positive	**Negative**		
Positive for Autoimmune diseases	9 (true positive)	2 (false positive)	11	**p<0.01**
Negative for Autoimmune diseases	2 (False negative)	52 (true negative)	54	
Total	**11**	**54**	**65**	
Positive for Malignant diseases	1(true positive)	1 (false positive)	2	**p<0.01**
Negative for Malignant diseases	0 (False negative)	63 (true negative)	63	
Total	**1**	**64**	**65**	
Positive for Inflammatory diseases	50 (true positive)	2 (false positive)	52	**p<0.01**
Negative for Inflammatory diseases	3 (False negative)	10 (true negative)	13	
Total	**53**	**12**	**65**	

Table IV presents that patient from 4 oral mucocutaneous diseases namely erythema multiforme, pemphigus vulgaris, pemphigus group, and squamous cell carcinoma show the maximum number of patients in the age group of 41-50. In contrast, only oral lichen planus and discoid lupus erythematosus show the highest number of patients in the age group of 31-40 years and 21-30 years, respectively. Oral lichen planus, pemphigus vulgaris, pemphigus group, and squamous cell carcinoma highlight the male predominance where erythema multiforme, discoid lupus

erythematosus, and systemic lupus erythematosus show female predominance. The highest 45 (69.23%) patients display buccal mucosa involvement where 31, 9, 2, 1, and 2 patients were belonging to oral lichen planus, erythema multiforme, pemphigus vulgaris, pemphigus group, and squamous cell carcinoma, respectively. In addition, 7 (10.76%), 6 (9.23%), 5 (7.69%), and 2 (3.07%) patients' tongue, gingiva, lip and palate were involved, respectively. In regards to histopathological findings, about 60 (92.3%) subjects had presented positive results where only 5 (7.69%) showed negative results.

Category		Oral Lichen Planus 34 (52.31 %)	Erythema multiforme 18(27.69%)	Pemphigus vulgaris 5 (7.69%)	Discoid lupus erythematosus 3(4.61 %)	Pemphigoid group 2 (3.08%)	Systemic lupus erythematosus 1 (1.54%)	Squamous cell carcinoma 2(3.08 %)	Total F (%)
Age	21-30	10	2	0	2	0	0	0	14 (21.54%)
	31-40	18	4	0	1	0	1	0	24 (36.92%)
	41-50	6	12	5	0	2	0	2	27 (41.54%)
Sex	Male	25	5	5	1	2	0	2	40 (61.53%)
	Female	9	13	0	2	0	1	0	25 (38.47%)
Location of oral involvement	Buccal Mucosa	31	9	2	0	1	0	2	45 (69.23%)
	Palate	0	0	0	1	0	1	0	2 (3.07%)
	Lip	0	2	1	2	0	0	0	5 (7.69%)

	Tongue	0	4	2	0	1	0	0	7 (10.76%)
	Gingiva	3	3	0	0	0	0	0	6 (9.23%)
Histopathological findings	Positive result	34	16	3	3	2	1	1	60 (92.3%)
	Negative result	0	2	2	0	0	0	1	5 (7.69%)

Table IV: Distribution of participants according to socio-demographic profile, oral involvement, and histopathological findings

4. Discussion

This prospective-observational study was carried out among 65 clinically diagnosed patients of oral mucocutaneous diseases at the department of Dermatology and Venereology and Department of Pathology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka. The purpose of this study was to conduct the clinical evaluation of oral mucocutaneous diseases and histopathological correlation.

The current study shows that oral mucosal diseases are more common in people over 30 years of age which is similar to some previous studies conducted among the dermatological patients [16, 17]. Prior authors reported female predilection for the incidence of this disease [16, 17] but this is contradicted by the present findings as male patients were higher than the female. However, another study report [18] upholds the male dominance like this study. The small sample size, low willingness to seek medical care and the patriarchal social system of Bangladesh may cause women to show a lower percentage than men in this study.

Like some earlier studies [19, 20], this study found more inflammatory oral mucocutaneous disease than autoimmune and malignant patients. This finding suggestive of occurring more inflammatory than the other types oral mucosal disease to the clinicians and other concerned persons dealing with oral mucocutaneous disease. However, this may vary depending on the geographic region as systemic autoimmune conditions are estimated to affect about 5% to 8% of Americans [21]. Therefore, a comprehensive nation-based study is recommended to carry out in this regard.

Oral lichen planus (OLP) was the most common of the other oral MCDs among participants in this study, which is consistent with another research [3]. This disease is usually occurred among the people above 30 years of age [18]. Similarly, the present statistics show that the maximum number of OLP affected patients was over 30 years of age. This type of oral MCDs is controversial in terms of

gender dominance because previous studies have noticed dominance of both men and women [18]. In contrast, the current research data pictures an opposed scenario for male and female ratio in the case of erythema multiforme because the number of affected females was higher than males here but the previous data [20] presents entire reverse information regarding this. Furthermore, even in the case of age-related prevalence of erythema multiforme, the data from this study are not supported by the results obtained in previous studies [20,21]. In the terms of age dominance for pemphigus vulgaris and group, the present study findings partially uphold a study conducted in 2015 by Kumar and colleagues [18]. However, in the case of gender prevalence for pemphigus vulgaris and group, a completely opposite picture can be noticed compared to this study with prior research [18]. Discoid lupus erythematosus (DLE) occurs at any age but most often develops in persons aged 20-40 years and women are 2-3 times more affected than men [22] which upholds the present study investigations. This study found only one female patient between the ages of 31-40 years in systemic lupus erythematous series which supports the results of other study [23] on the frequency of age and gender occurrence but these results cannot be generalized due to small samples. Furthermore, this statement also applies to squamous cell carcinoma because there were only 2 patients in this series of this study. Thus, it is being requested to conduct research on the basis of socio-demography of oral mucocutaneous diseases on a larger scale individually.

Regarding the distribution of mucosal lesions in the oral cavity, different sites in oral cavity show predilection for different types of lesions. The site of the lesion is also an important etiological factor. Unlike some earlier authors report [18, 25], buccal mucosa (69.23% of cases) was identified as the most common site of oral involvement for this research like a study carried out by Kamble et al. (2017) [25]. On the other hand, nearly half of the participants showed buccal mucosa involvement in the research report of Ali et al. (2013) [26] but the tongue and hard palate were identified as the most common sites of occurrence of oral mucosal lesions by Mansour Ghanaei et al. (2013) [27] and Patil et al. (2015) [28] directed research report, respectively. Further, gingiva was identified as the second common site of oral involvement in some prior studies [18]. However, tongue, gingiva, lip, and palate were affected in 10.77%, 9.23%, 7.69%, and 3.07% of cases in the present study.

During complicated, severe or doubtful cases, histopathological examination is suggested by the clinicians. This study showed that positive histopathological results were found in about 92.3% of cases for all oral mucosal diseases except erythema multiforme, pemphigus vulgaris, and squamous cell carcinoma. Both positive and negative results have been found for the three disorders mentioned above. In addition, a statistical significance ($p<0.01$) was found between the clinical diagnosis and histopathological findings of the diseases in this study. Since there are no distinct and obvious clinical manifestations of oral mucosal disease and overlapping of positive and negative histopathological outcomes can be observed, thus, clinicians are advised to perform both clinical and microscopic examinations for accurate diagnosis of oral mucocutaneous disease.

5. Conclusion:

Based on the histopathological diagnosis of oral lesions in this study, it can be concluded that clinical diagnosis cannot be used as a reliable tool with which mucocutaneous diseases can be diagnosed and

thus, histopathological examination should be done to plan the appropriate management in majority of cases.

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